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09/623,514	03/29/2001	Jitao Zou	43922	8673
24247	7590	01/16/2004		
TRASK BRITT P.O. BOX 2550 SALT LAKE CITY, UT 84110			EXAMINER BAUM, STUART F	
			ART UNIT	PAPER NUMBER
			1638	

DATE MAILED: 01/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/623,514

Applicant(s)

ZOU ET AL.

Examiner

Stuart F. Baum

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 22 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-33 is/are pending in the application.
- 4a) Of the above claim(s) 5,7 and 22 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 8 and 9 is/are allowed.
- 6) ☐ Claim(s) 2,4,12,13,32 and 33 is/are rejected.
- 7) ☐ Claim(s) 1,3,6,10,11,14-21 and 23-31 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***RCE Acknowledgment***

1. The request filed on September 22, 2003 for a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114, based on parent Application No. 09/623,514 is acceptable and a RCE has been established. An action on the RCE follows.

2. Claims 1-33 are pending.

Claims 5, 7, and 22 have been withdrawn from consideration because the claims are drawn to non-elected inventions.

Claims 32-33 have been newly added.

3. Claims 1-4, 6, 8-21, 23-33 are examined in the present office action.

### ***Claim Objections***

4. Claim 1 is objected to for reciting an improper article. On line 3, the second "a" should be replaced with --the--.

Claim 2 is objected to for reciting an improper article. On line 5, the second "the" should be replaced with --a--.

Claims 2, and 4 are objected to for reciting "identity" instead of "sequence identity".

Claim 3 is objected to for reciting an improper article. On line 3, the article "a" should be replaced with --the--.

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Claim 4 is objected to for reciting an improper article. On line 6, the first recitation of the article "the" should be replaced with --a--.

Claim 10 is objected to for reciting an improper article. On line 3, the article "a" should be replaced with --the--.

Claim 11 is objected to for reciting an improper article. On line 3, the article "a" should be replaced with --the--.

Claims 12 and 13 are objected to for reciting an improper article. On line 1, the second recitation of the article "a" should be replaced with --the--. Plants only have one genome.

Claims 14-18 are objected to for improper grammar. On line 3, the phrase "grown in identical conditions" should follow the phrase "plants of the same genotype" which it is modifying. In addition, the conjunction "but" should be inserted before the word "without".

Claim 19 is objected to for reciting an improper article. On line 2, the second recitation of the article "a" should be replaced with --the--. Plants only have one genome.

Claim 19 is objected to for reciting an improper article. On line 4, the recitation "a" should be replaced with --the--.

Claim 23 is objected to for reciting an improper article. On line 7, the recitation "a" should be replaced with --the--. Plants only have one genome.

Claims 33 is objected to for inadvertently reciting "of" on line 1, instead of "or".

***Written Description***

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 2, 4, 12-13, and 32-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to an isolated nucleic acid molecule encoding a polypeptide having diacylglycerol acyltransferase activity, wherein the nucleic acid molecule comprises a sequence that is a fragment of SEQ ID NO:1 or 3 and wherein the fragment exhibits 90% sequence identity with SEQ ID NO:1 or 3, a vector comprising an above recited sequence, a plant or plant seed transformed therewith, or the claims are drawn to an isolated nucleic acid molecule encoding a polypeptide having diacylglycerol acyltransferase activity wherein the sequence is a fragment of SEQ ID NO:1 or 3.

Applicants disclose SEQ ID NO:1 which is an isolated DGAT cDNA clone from an *Arabidopsis* cDNA library made from RNA isolated from silique-specific tissue (page 19, line 2). The DGAT cDNA clone was obtained by amplifying a DGAT sequence using primers designed from a genomic sequence. A clone was amplified that contained 1904 nucleotides and contained an ATG at position nt-139 (page 19, line 10). Applicants also disclose the DGAT genomic sequence of SEQ ID NO:3 (page 33, and Sequence listing).

Applicants do not identify essential regions of the DGAT cDNA or genomic sequence nor do Applicants describe any fragments of SEQ ID NO:1 or 3 that exhibit 90% identity with SEQ

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ID NO:1 or 3 that have diacylglycerol acyltransferase activity. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of nucleic acid sequences encoding a polypeptide having diacylglycerol acyltransferase activity falling within the scope of the claimed genus of sequences. Applicants only describe one cDNA sequence and the corresponding genomic sequence. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of sequences encoding a polypeptide having diacylglycerol acyltransferase activity. Hence, Applicants fail to meet either prong of the two-prong test set forth by Eli Lilly. Furthermore, given the lack of description of the necessary domains essential for a polypeptide having diacylglycerol acyltransferase activity, it remains unclear what features identify a nucleic acid sequence encoding a polypeptide having diacylglycerol acyltransferase activity. Since the genus of nucleic acid sequences encoding a polypeptide having diacylglycerol

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acyltransferase activity have not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

### ***Scope of Enablement***

6. Claims 2, 4, 12-13, and 32-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to a DGAT cDNA clone of SEQ ID NO:1 from *Arabidopsis* transformed into wild-type *Arabidopsis* to yield plants with an increased oil content (page 24, line 19) an increase seed weight and an oil content that exhibited a decrease in the total saturates and an increase in the monounsaturates (page 24, line 23) does not reasonably provide enablement for claims broadly drawn to an isolated nucleic acid molecule encoding a polypeptide having diacylglycerol acyltransferase activity, wherein the nucleic acid molecule comprises a sequence that is a fragment of SEQ ID NO:1 or 3 and wherein the fragment exhibits 90% sequence identity with SEQ ID NO:1 or 3, a vector comprising an above recited sequence, a plant or plant seed transformed therewith, or an isolated nucleic acid molecule encoding a polypeptide having diacylglycerol acyltransferase activity wherein the sequence is a fragment of SEQ ID NO:1 or 3. and plants and plant seeds exhibiting an altered seed oil content, an altered diacylglycerol content, an altered fatty acyl composition, and an enhanced biomass. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists

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a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The Applicants isolated a DGAT cDNA clone from an *Arabidopsis* cDNA library made from RNA isolated from silique-specific tissue (page 19, line 2) by amplifying a DGAT sequence using primers designed from a genomic sequence. A clone was amplified that contained 1904 nucleotides and contained an ATG at position nt-139 (page 19, line 10). Applicants believe this to be a full length clone and it was designated as SEQ ID NO:1. Expressing this sequence in yeast resulted in an increase in DGAT activity and this sequence complemented a mutant DGAT gene in *Arabidopsis* (page 23, line 30).

The instant specification fails to provide guidance for which fragments of SEQ ID NO:1 or 3 would have diacylglycerol acyltransferase activity and exhibit 90% identity with SEQ ID NO:1 or 3. Applicants have not taught how one skilled in the art, would identify and isolate such fragments. Applicants have only disclosed and used the full length sequence of SEQ ID NO:1 but Applicants have not exemplified any fragments of SEQ ID NO:1 or 3 that can be used in Applicants invention and that are encompassed by Applicants claims drawn to fragments exhibiting 90% identity with SEQ ID NO:1 or 3 and exhibiting diacylglycerol acyltransferase activity.



The specification also fails to provide guidance for which amino acids of SEQ ID NO:1 or 3 can be altered, and which amino acids must not be changed, to maintain activity and substrate specificity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and still produce a functional enzyme.

It cannot be predicted by one of skill in the art that sequences encoding a fragment of SEQ ID NO:1 or 3 will catalyze a reaction with the same activity and substrate specificity as the DGAT enzymes of SEQ ID NO:1 or 3. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by McConnell et al (2001, Nature 411 (6838):709-713), who teach that the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain. This change renders the protein constitutively active and

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therefore creates a dominant mutation which has a drastic alteration in phenotype compared to wild-type *Arabidopsis* plants.

Wiberg, et al (1994, *Phytochemistry* 36(3):573-577) teach that DGAT from seeds of *Cuphea procumbens* selectively utilize DAG acyl-CoA species with a ten atom carbon tail with no saturations (10:0) but that DGAT from castor bean selectively utilizes a 18:1 acyl-CoA species. Wiberg et al concludes by stating that DGAT enzymes from some oil seeds can discriminate between various alterations of the acyl-CoA substrate (page 575, left column, 4<sup>th</sup> paragraph). The different substrate specificities of the DGAT enzyme are a consequence of the amino acid variability between the various isoforms of the DGAT enzyme. Therefore, a knowledge of which amino acids are essential for proper substrate specificity is required when determining which amino acids to change, delete or rearrange within the protein sequence.

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of SEQ ID NO:1 or 3 as probes or by designing primers to undisclosed regions of SEQ ID NO:1 or 3 and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when over-expressed have diacylglycerol acyltransferase activity and exhibit 90% identity with SEQ ID NO:1 or 3.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

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7. Claims 1-4, 6, 8-21, and 23-33 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated polynucleotide of SEQ ID NO:1 or SEQ ID NO:3 encoding SEQ ID NO:2 or sequences having 90% sequence identity to SEQ ID NO:1 or 3 wherein the sequence encodes a polypeptide having diacylglycerol acyltransferase activity and plant transformed therewith.

8. Claims 8-9 are allowable.

9. Claims 1, 3, 10-11, 14-19 and 23 are objected to but would be allowable if the objection is corrected.

10. Claims 6, 20-21, 25, 28-31 are objected to for depending on an objected base claim.

11. Claims 24, and 26-27 are objected to for being dependent on a rejected base claim.

12. Claims 2, 4, 12-13, and 32-33 are rejected.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 703-305-6997 or after January 6, 2004, 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 703-306-3218. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Stuart F. Baum Ph.D.

January 5, 2004

A handwritten signature in black ink, appearing to read "Amy Nelson", written in a cursive style.

AMY J. NELSON, PH.D  
SUPERVISORY PATENT EXAMINER  
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